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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/796,509

03/09/2004

Guiying Li

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1959

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09/30/2004

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EXAMINER

BERCH, MARK L

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/796,509

Applicant(s)

LI ET AL.

Examiner

Mark L. Berch

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-78 is/are pending in the application.
- 4a) Of the above claim(s) 1-64 and 66-78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 65 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claim 1-64, 74-78, drawn to Compounds and compositions, classified in class 544, subclass 281.
- II. Claims 65, drawn to treatment of anxiety, depression, sleep disorder, ADD, or Alzheimer's Disease, classified in class 514, subclass 259.3.
- III. Claim 66, drawn to method of potentiating another drug, classified in class 514, subclass various.
- IV. Claims 67-69, drawn to method of analysis, classified in class 436, subclass 503.
- V. Claims 70-73, drawn to method altering the activity of a receptor, classified in class 514, subclass 259.3.

The inventions are distinct, each from the other because of the following reasons:

The methods are fundamentally different from each other. Only Group II involves using the drug to treat a disease. Group III involves using the drug to potentiate the effect of another drug, and thus unlike other groups, requires an additional drug. Group IV is an analytical method. Group V requires that a receptor be altered, but does not require that any disorder be treated.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

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During a telephone conversation with Steve Sarussi on 9/23/2004 a provisional election was made with traverse to prosecute the invention of Group II, claim 65. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-64, 66-78 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 65 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anxiety, depression, and ADD, does not reasonably provide enablement for Alzheimer's Disease, sleep disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims, insofar as they embrace Alzheimer's Disease, sleep disorders generally, as not enabled.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation

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is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims.

A) Scope of genus. Owing to the broad range of the R1, R2, R3, R4, R6 and W, trillions of compounds are covered.

B) Scope of use. Alzheimer's Disease is one disorder. The extremely diverse range of sleep disorders covers Dyssomnias, Parasomnias, Medical/Psychiatric Sleep Disorders and others. First there are the Intrinsic Sleep Disorders, including Psychophysiological Insomnia, Sleep State Misperception, Idiopathic Insomnia, Narcolepsy, Recurrent Hypersomnia, Idiopathic Hypersomnia, Posttraumatic Hypersomnia, Obstructive Sleep Apnea Syndrome, Central Sleep Apnea Syndrome, Central Alveolar Hypoventilation Syndrome, Periodic Limb Movement Disorder, Restless Legs Syndrome, and Intrinsic Sleep Disorder NOS. Second there are the Extrinsic Sleep Disorders, including Inadequate Sleep Hygiene, Environmental Sleep Disorder, Altitude Insomnia, Adjustment Sleep Disorder, Insufficient Sleep Syndrome, Limit-Setting Sleep Disorder, Sleep-Onset Association Disorder, Food Allergy Insomnia, Nocturnal Eating (Drinking) Syndrome, Hypnotic-Dependent Sleep Disorder,

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Stimulant-Dependent Sleep Disorder, Alcohol-Dependent Sleep Disorder, Toxin-Induced Sleep Disorder, and Extrinsic Sleep Disorder NOS. Third, there are Circadian Rhythm Sleep Disorders, including Time Zone Change (Jet Lag) Syndrome, Shift Work Sleep Disorder, Irregular Sleep-Wake Pattern, Delayed Sleep Phase Syndrome, Advanced Sleep Phase Syndrome, Non-24-Hour Sleep-Wake Disorder, and Circadian Rhythm Sleep Disorder NOS. Fourth, there are Arousal Disorders, including Confusional Arousals, Sleepwalking, and Sleep Terrors. Fifth, there are Sleep-Wake Transition Disorders, including Rhythmic Movement Disorder, Sleep Starts, Sleep Talking, and Nocturnal Leg Cramps. Sixth, there are Parasomnias Usually Associated with REM Sleep, including, Nightmares, Sleep Paralysis, Impaired Sleep-Related Penile Erections, Sleep-Related Painful Erections, REM Sleep Related Sinus Arrest, and REM Sleep Behavior Disorder. Seventh, there are Other Parasomnias, including Sleep Bruxism, Sleep Enuresis, Sleep-Related Abnormal Swallowing Syndrome, Nocturnal Paroxysmal Dystonia, Sudden Unexplained Nocturnal Death Syndrome, Primary Snoring, Infant Sleep Apnea, Congenital Central Hypoventilation Syndrome, Sudden Infant Death Syndrome, Benign Neonatal Sleep Myoclonus, and Other Parasomnia NOS. Eighth, there are Sleep Disorders Associated with Mental Disorders, including Psychoses, Mood Disorders, Anxiety Disorders, Panic Disorder and Alcoholism. Ninth, there are Sleep Disorders Associated with Neurological Disorders, including, Cerebral Degenerative Disorders, Dementia, Parkinsonism, Fatal Familial Insomnia, Sleep-Related Epilepsy, Electrical Status Epilepticus of Sleep, and Sleep-Related Headaches. Tenth, there are Sleep Disorders Associated with Other Medical Disorders, including, Sleeping Sickness, Nocturnal Cardiac Ischemia, Chronic

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Obstructive Pulmonary Disease, Sleep-Related Asthma, Sleep-Related Gastroesophageal Reflux, Peptic Ulcer Disease and Fibrositis Syndrome. In addition, there are an assortment of poorly defined disorders and syndromes, including Short Sleeper, Long Sleeper, Subwakefulness Syndrome, Fragmentary Myoclonus, Sleep Hyperhidrosis, Menstrual-Associated Sleep Disorder, Pregnancy-Associated Sleep Disorder, Terrifying Hypnagogic Hallucinations, Sleep-Related Neurogenic Tachypnea, Sleep-Related Laryngospasm, and Sleep Choking Syndrome.

(2) The nature of the invention and predictability in the art: The invention is directed toward the treatment of disease and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. Page 41, page 13 gives a fairly large 1400 fold range. The dosage information that is provided is moreover generic, that is, it is not linked to any specific disease, an important consideration given the uge range of disorders mentioned in the specification..

(4) State of the Prior Art: Broadly speaking, these compounds are pyrazolo[1,5-a]pyrimidines with a particular substituent type at the 2-position. So far as the examiner is aware, no pyrazolo[1,5-a]pyrimidines compounds of any kind are in actual use for Alzheimer's Disease or any sleep disorder, let alone sleep disorders generally. Further, there is still a great deal of research going on trying to figure out how Alzheimer's Disease arises. The channel hypothesis of Alzheimer's disease proposes that the beta-

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amyloid peptides which accumulate in plaques in the brain actually damage and/or kill neurons by forming ion channels. An abnormal phosphorylation of tau proteins is being investigated as one of the important events in the process leading to their aggregation. There appears to be a specific alteration of a p53-mediated intracellular pathway involved in sensing and repairing DNA damage in peripheral cells, and the role of neuronal apoptosis is under investigation. MOCA (previously called presenilin [PS] binding protein) appears to have a significant effect on beta-amyloid precursor protein secretion. Other investigations have focused on β - and γ -secretase inhibitors, A β vaccination, Cu-Zn chelators, cholesterol-lowering drugs, PPlase binding compounds (a class of rotamase inhibitors), and non-steroidal anti-inflammatory drugs. Many, many other lines of research are being pursued because there is no clear understanding of the Alzheimer's Disease mechanism. As for sleep disorders, these are so diverse that there is no overall mechanism that underlies all these or even most of these.

(5) Working Examples: There are no working examples of treatment of any disorder at all.

(6) Skill of those in the art: The skill level for Alzheimer's Disease is considered low. Alzheimer's Disease is an extraordinarily difficult disease to treat, and has been the subject of a vast amount of research. Despite an enormous number of different approaches, the skill level in the art is so low relative to the difficulty of task that the only success has come from treatment by compounds which are Acetylcholinesterase inhibitors (Aricept®, Cognex®, Exelon®, and Reminyl®), or voltage-dependent NMDA-antagonists (Memantine), properties these compounds are not disclosed to have. Indeed, GABA_A is not currently even considered an important research area. As for

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sleep disorders, the great majority of these cannot be treated with pharmaceuticals, and those that are are generally treated by attaching to original cause. Thus, for Sleep Disorders Associated with Mental Disorders, e.g. Psychoses, this would be treated by giving an anti-psychotic medication.

(7) The quantity of experimentation needed: Owing to the factors listed above, especially in points 1, 4 and (6), experimentation needed will be extensive. Alzheimer's Disease treatments are well known to be among the most difficult to test. This is in part due to the fact that there is no good physiological test for Alzheimer's Disease; one must rely on assorted psychological tests.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claim Objections

Claim 65 is objected to as dependent on a non-elected claim. This can be fixed by placing claim 65 in independent form.

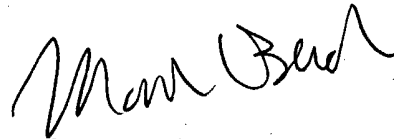
The abstract is objected to; it needs mention of the disorders being claimed here.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on (571)272-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at 571-272-0661. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

A handwritten signature in black ink, appearing to read "Mark L. Berch", is positioned above the printed name.

Mark L. Berch
Primary Examiner
Art Unit 1624

September 28, 2004